



April 29, 2002

Food and Drug Administration
Dockets Management Branch, HRA-305
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Subject: Draft Guidance entitled, "Guidance for Industry: Use of Nucleic Acid Tests on Pooled Samples from Source Plasma Donors to Adequately Reduce the Risk of Transmission of HIV-1 and HCV," Dated December 2001, Docket No. 01D-0584

Dear Sir or Madam:

Nabi is pleased to provide these comments on the Food and Drug Administration's (FDA's) draft guidance entitled, Guidance for Industry: Use of Nucleic Acid Tests on Pooled Samples from Source Plasma Donors to Adequately Reduce the Risk of Transmission of HIV-1 and HCV," Dated December 2001 (hereinafter "Draft Guidance").

1. **Applicability of Draft Guidance:** The directed audience of the draft guidance is not always clear. Although the introduction addresses "you" to be establishments engaged in the manufacture of Source Plasma, later references in the document simply state "manufacturers" and "establishments." Some of those references are to the Source Plasma manufacturers/establishments, but others reference manufacturers of NAT tests. Fractionators are another form of "manufacturer" recognized by the reader of this guidance document. Because implementation of NAT testing as a requirement for the Source Plasma manufacturer changes the paradigm of testing in this industry, i.e., currently nearly all Source Plasma is being NAT tested but the majority of the testing is customer (fractionator) controlled, rather than collector controlled, clarity of intention and redundancy in the document is desirable. Whenever "manufacturer" is referenced, it should be specified to which manufacturer it applies, e.g., "manufacturer of Source Plasma," and whenever "establishment" is referenced, it would be helpful to spell out, "establishments that manufacture Source Plasma" if that is the directed audience. Because of the business/contract arrangements now in place for the NAT testing to be performed by the customer, rather than the supplier, the guidance needs to be clear and unambiguous in all sections concerning who is to be responsible for NAT testing of Source Plasma.

Knowledge of the referenced regulation under which this draft guidance is published [21 CFR 610.40(b)] provides information that the intention of this draft guidance is to require NAT testing as a release test for Source Plasma. However, because of the current industry practices and the current state of NAT testing [one licensed test manufacturer/laboratory and long testing turnaround times (TAT)], it is suggested that FDA consider whether an alternative testing strategy would

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accomplish the same goal without disrupting the dynamics that have developed between the collection facilities and fractionators prior to the release of the FDA draft guidance.

In a perfect world, I think we would all agree that NAT testing prior to release of the Source Plasma would be preferred. However, we may not be there yet technologically and logistically. In an ideal situation, the NAT test results would be transmitted to the plasma collection facility at the same time the other viral marker tests are completed. Most viral marker test results are returned to collection centers within 7 – 10 days of the collection date. TATs for NGI's NAT testing are more in the 30-day time frame. Other investigational NAT tests take even longer. Resolution of discordant pool testing adds additional time and because of the large pools, may leave test results for a large number of units (those in the pools and subsequent bleeds from donors whose bleeds require test resolution) in limbo. Because of TATs for NAT, for serial Source Plasma donors, it is not the NAT testing that defers the donors and initiates product retrieval and look back. Usually, the donor has been deferred on the basis of viral marker test results or ALT before the collection center receives the positive NAT result. Requiring NAT testing as a pre-release test for Source Plasma will cause disruption in storage and shipping—again, because of the TATs. Until TATs can be improved—hopefully, in combination with the licensing of additional test laboratories to guard against potential problems with laboratory contamination or other processing disruptions, it may be premature to require NAT testing as a pre-release test for Source Plasma. For these reasons, it is suggested that FDA consider as an interim strategy the continuation of NAT testing controlled by the fractionator as a necessary test prior to using the unit of plasma in manufacturing (i.e., pooling).

2. Labeling: If it is determined that NAT testing will be a required test for release of the Source Plasma, it is recommended that FDA provide a section in the document on labeling requirements.
3. Content of BLA: It would be helpful if the guidance would elaborate more on the content of any BLA supplement filing and the category for filing BLA supplements. Of course, the BLA filing is dependent upon who controls the testing, i.e., the Source Plasma collector or the fractionator. Even with fractionator-controlled testing, there are novel licensing strategies utilizing contract manufacturing agreements that may place ultimate responsibility on the collector without disrupting the current testing models and distribution of plasma. If the guidance document provided acceptable scenarios, it would save the agency and industry time and resources.
4. Test of Record: In the implementation paragraph, there has been much confusion about the meaning of the sentence, “After we approve the supplement for use. . .at the same time.” Does this statement mean that duplicate testing will be required using the licensed test and the test under IND? Because of the TATs discussed

above and the use of other required viral marker and related tests, please consider whether duplicate NAT testing is warranted or desirable at this time.

5. General Comment for Any Draft Guidance: Stating an implementation date in a draft guidance document leads one to believe that the draft guidance is to be implemented, as is, by that date. It would be better to state in the draft that implementation should occur within six months of issuance of the final guidance. The inclusion of the June 1, 2002 date in the draft guidance is particularly disconcerting since the comment period does not close until May 1, 2002. International customers are most confused by dates in drafts because they do not understand GGP/guidance document rules. To them, any document from FDA is a directive, and they do not understand that the June 1 date is not firm.

Nabi appreciates the opportunity to comment on this draft guidance. Should you have any questions regarding these comments or would like additional information, please contact me.

Sincerely,

A handwritten signature in black ink, appearing to read 'Mary Gustafson', with a stylized flourish at the end.

Mary Gustafson
Senior Director
Regulatory Affairs/Plasma

align

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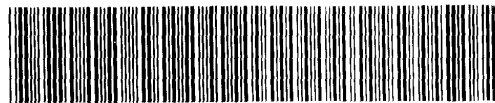


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